REMARKS

In response to the Office Action dated August 8, 2007, Applicants submit the following remarks.

The three-month extended deadline for filing a response falls on February 8, 2008. A three-month Petition for Extension of Time and the required fee are filed herewith; therefore, Applicants believe that this response is being timely filed. In the event that there are any additional fees required in connection with this response, please charge any necessary fee to Deposit Account No. 23-2415, referencing Docket No. 30797-717.201.

I. Applicants acknowledge withdrawal of the following rejections:

1. The rejection of claims 8, 9, 10 and 11 under 35 U.S.C. 112, first paragraph as for allegedly failing to be sufficiently enabled for EGF;
2. The rejection of claims 8, 9, 10 and 11 under 35 U.S.C. 112, first paragraph for allegedly failing to comply with the written description requirement;
3. The rejection of claims 1, 2 and 4-13 under 35 U.S.C. 112, first paragraph for allegedly a lack of enablement of vaccines;
4. The rejection of claims 1, 2 and 4-13 under 35 U.S.C. 112, first paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention in view of the amendments to the claims.
5. The provisional rejection of claims 1, 2 and 4-13 for obviousness–type double patenting.
6. The rejection of claims 1, 10 and 11 under 35 U.S.C. 103(a) as allegedly unpatentable over Hoeprich in view of Gonzalez, Gonzalez-1997, or Gonzalez-1998, and further in view of De Luca.

II. The Examiner has maintained the following claim rejections:

1. Claims 1 and 2, 7 and 12 are/remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoeprich (Hoeprich, Jr., P.D. et al., The Journal of Biological Chemistry, 254(32): 19086-19091, 1989; of record) in view of Gonzalez (Gonzalez et al. Scandinavian J. Immunol., 52: 113, August 2000).

Claim 1 recites:

> A composition containing human TGFα "hTGFα", wherein said hTGFα comprises the amino acid sequence of SEQ ID NO 2 or its combination with other EGF-R ligands, coupled with a carrier protein by genetic cloning before expression of said proteins or by chemical conjugation after expression of said proteins, wherein said composition contains an adjuvant, wherein said composition is able to produce a specific immune response against said hTGFα, and wherein said carrier protein is P64k.

As previously stated of record, Hoeprich does not teach or suggest a vaccine composition wherein the carrier protein is P64k as currently recited by the claims.

Also previously stated was the fact that the present application was filed on December 6, 2001 and claims priority to Cuban Application No. 286/2000, filed December 6, 2000 as evidenced by the filing receipt. The Gonzalez reference was published in August 2000 and, thus, is a § 102(a) publication date (i.e., less than a year prior to the effective filing date of the present application).

Applicants previously submitted a 37 CFR § 1.131 Declaration by inventor Belinda Sánchez Ramírez and an attached laboratory notebook page, previous Exhibit B, demonstrating that the fusion proteins as claimed were conceived and reduced to practice prior to the August 2000 publication date of the Gonzalez reference.

Briefly, the expression vector pM 92 was used to generate the hTGFα-P64K fusion protein, and FIG. 2 of the present application shows a schematic representation of the expression vector obtaining process. This vector codes for the fusion protein TGFα-P64K which was made using techniques described in the laboratory notebook page of Exhibit B.

In the present Office Action, the Examiner alleges:

> ...the page from the laboratory notebook is in the Spanish language. Furthermore, what can be gleaned from Exhibit B is that some procedure was performed with a nucleic acid encoding for TGF alpha and with a vector referred to a [sic] pM92. However, one cannot discern from the notebook page that a fusion between TGFα and P64K was made or contemplated because the term p64K or IpdA (the gene coding for P64K protein from Neisseria meningitides (strain B385)) does not appear anywhere in Exhibit B.

[8/8/07 Office Action at p. 6]. Applicants respectfully disagree. However, Applicants provide herewith copies of additional pages of a laboratory notebook from the inventors that clearly describe the pM92 vector as containing the IpdA gene.

Firstly, as evidenced by Silva et al., FEMS Microbiology Letters, 174: 191-199 (1999), and attached herewith as Exhibit C, the IpdA gene encodes P64K (see abstract & introduction, pp. 1919-92).

Secondly, Exhibit D, filed herewith, is a copy of two pages from the inventors' laboratory notebook where the first page (page 14, dated May 13, 1999 in the upper right-hand corner) describes the use of pMTGF plasmid to express the TGFα-P64K fusion protein encoded by this plasmid. The plasmid map for pM92 is found on the next page of the Exhibit. Despite the Spanish language of the notebook, the plasmid map clearly identifies (1) the plasmid pM92 (see upper right plasmid) which contains the IpdA gene within pM92, (2) the plasmid pSK containing

the gene for human TGFα (see upper left plasmid), and (3) the resultant pMTGF plasmid which contains the fusion protein between TGFα and the IpdA gene. In the final plasmid, pMTGF, the TGFα gene is clearly identified as fused with the IpdA gene. As shown above, the IpdA gene is known to encode the P64K protein of *Neisseria meningitides*. Thus, Applicants assert that these laboratory notebook pages conclusively demonstrate the conception and reduction to practice of the TGFα-P64K fusion protein compositions as presently claimed at least by May 1999, and the compositions as claimed antedate the August 2000 publication date of Gonzalez et al.

Furthermore, the second laboratory notebook page attached herewith as Exhibit E demonstrates conception and possession of the TGFα-P64K fusion protein by the inventors prior to the August 2000 publication of Gonzalez et al. In particular, page 23 of the laboratory notebook (dated August 13, 1999 in the upper right-hand corner of the page) describes the expression of pMTGF (described above and in Exhibit B) in *E. coli* bacterial cells. Specifically, the description of the figure at the bottom of the page explicitly identifies the expression of the fusion protein "TGFalpha-P64K" in *E.coli*, referring to the expression of TGFα-P64K fusion protein encoded by the pMTGF plasmid. While the notebook page is, again, in Spanish, the reference to the expression of the TGFα-P64K fusion protein is very clear and easily identified. Thus, Applicants assert that this laboratory notebook page provides additional evidence of the conception and reduction to practice of the TGFα-P64K fusion protein compositions as presently claimed prior to the August 2000 publication date of Gonzalez et al. Further provided herewith is a declaration by inventor Belinda Sánchez Ramírez in support of the arguments above.

In conclusion, Applicants submit that, in view of the declaration by inventor Belinda Sánchez Ramírez and the supporting objective evidence, Gonzalez does not qualify as a prior art reference. In addition, the Hoeprich reference fails to teach each and every element of the currently recited claims. Hoeprich cannot, therefore, anticipate or render obvious the claims as currently recited.

Applicants respectfully request reconsideration and withdrawal of the rejection.

7. Claims 1, 4-6, 12 and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoeprich (Hoeprich, Jr., P.D. et al., The Journal of Biological Chemistry, 254(32): 19086-19091, 1989; of record) in view of Gonzalez (Gonzalez et al., Scandinavian J. Immunol., 52: 113, August 2000) and further in view of Gonzales (Gonzales et al., Vaccine Research, 6(2): 91-100, 1997; of record).

Hoeprich and Gonzalez (August 2000) have been addressed *supra*. Applicants submit that, in view of the declaration by inventor Belinda Sánchez Ramírez and the supporting objective evidence, Gonzalez does not qualify as a prior art reference. Further, the Hoeprich reference fails to teach each and every element of the currently recited claims; Hoeprich cannot, therefore, anticipate or render obvious the claims as currently recited alone, or in combination with Gonzales and respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Applicants respectfully request prompt and favorable action with regard to pending claims 1, 2, 4-7 and 12-13. Further, Applicants respectfully request rejoinder and allowance of amended method claims 14-18.

The Applicants further submit these remarks with a Request for Continued Examination in response to the Final Office Action dated August 8, 2007. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 23-2415 and please credit any excess fees to such deposit account.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2300.

Respectfully submitted,

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